Supplementary Fig. 1

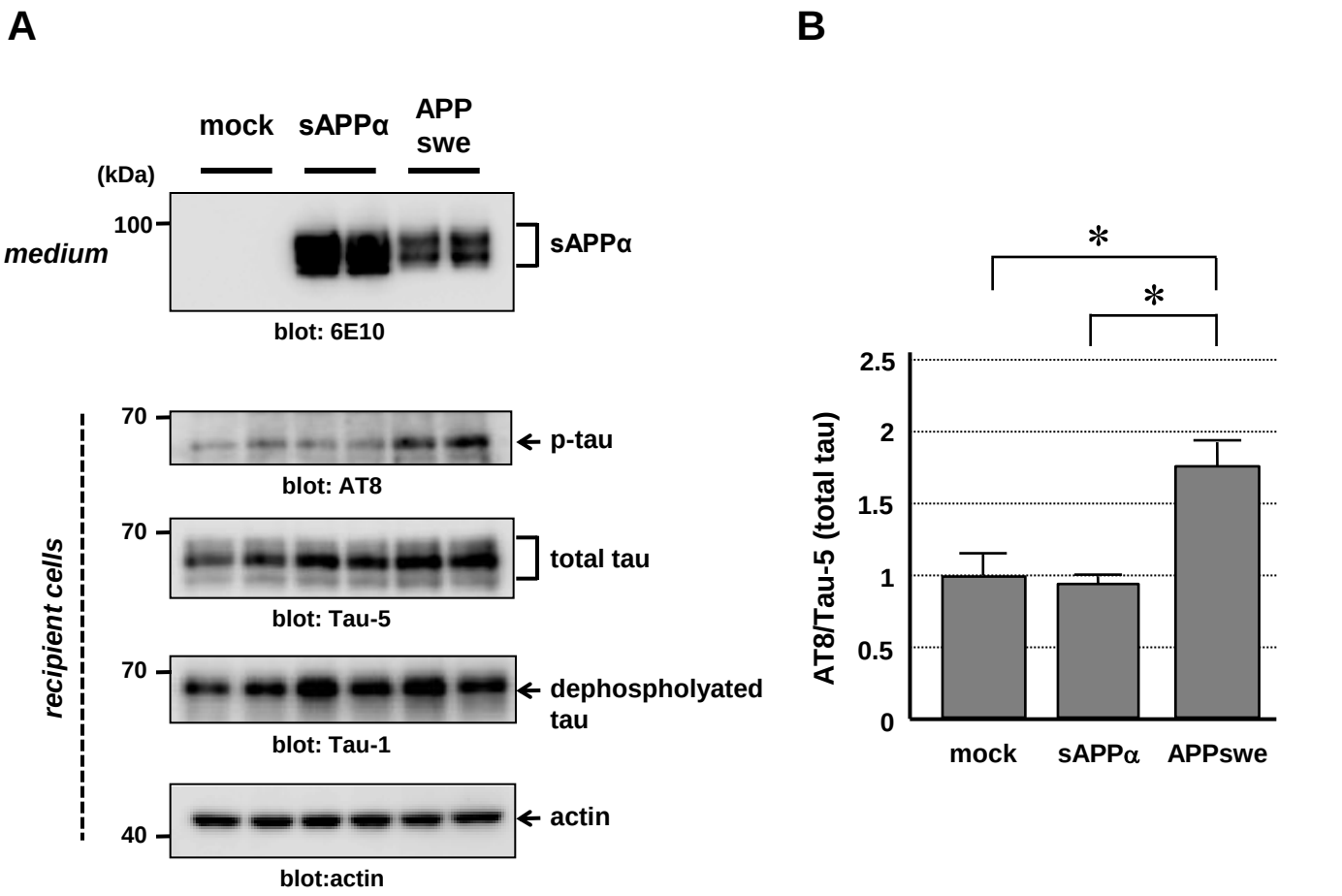

Figure legends

(A) Donor HEK293 cells were transiently transfected with cDNA encoding the vector only (mock), sAPPα, or APPswe. Expression of sAPPα and APPswe in the donr cells yielded a substantial amount of sAPPα in the medium. Expression of APPswe that produced high amounts of Aβ in the medium resulted in an increased level of phosphorylated tau in the N2a recipient cells. In contrast, the level of phosphorylated tau in the recipient cells cocultured with the donor cells expressing sAPPα was comparable to that of mock-transfected cells.

(B) Semiquantitative analysis of AT8 /Tau-5 (total tau) revealed that the level of phosphorylated tau in the recipient cells cocultured with APPswe-expressing donor cells was significantly higher than that in the recipient cells cocultured with mock- or sAPPα-transfected donor cells. *$P<0.05$ by Tukey's test after ANOVA.

Supplementary Fig. 2

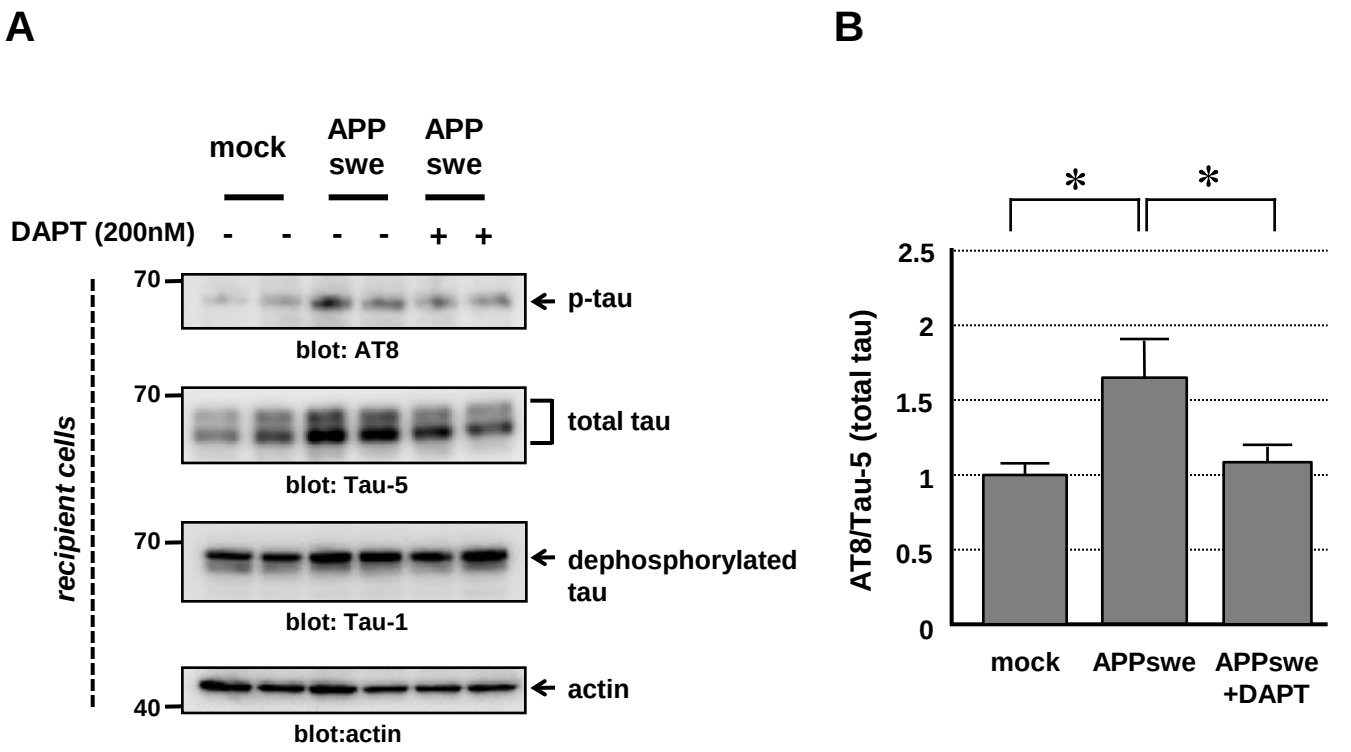

Figure legends

(A) The recipient N2a cells were cocultured with donor HEK293 cells treated with vehicle only or the γ-secretase inhibitor DAPT (200 nM). Detergent-extracted lysates of the recipient N2a cells were analyzed using the indicated antibodies. The level of phosphorylated tau decreased in the presence of DAPT.

(B) Semiquantitative analysis of AT8/Tau-5 (total tau) revealed that the phosphorylation of exogenous tau in the recipient cells was significantly blocked by the treatment with DAPT. *$P<0.05$ by Tukey's test after ANOVA.

Supplementary Fig. 3

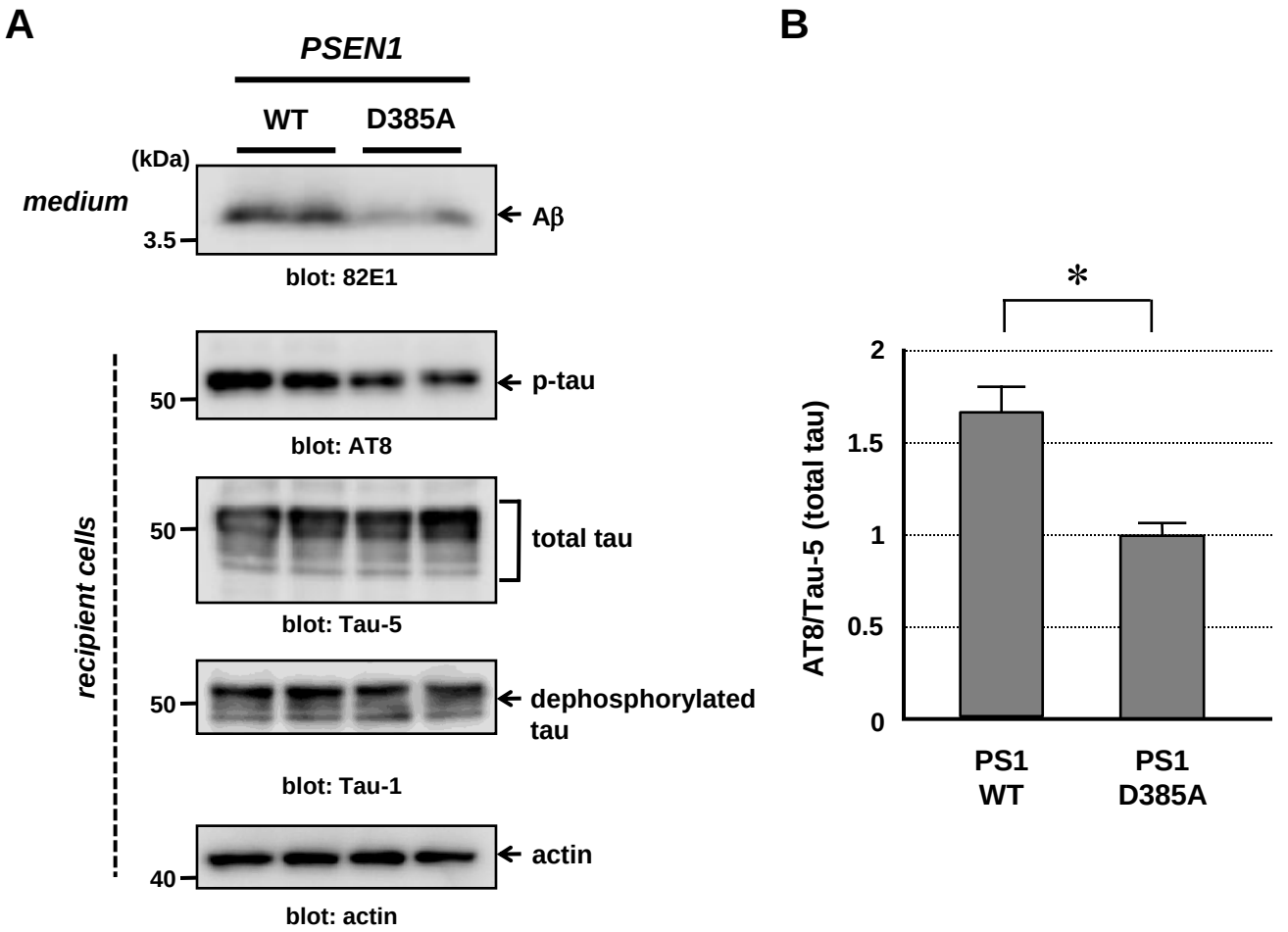

Figure legends

(A) Donor HEK293 cells stably expressing WT *PSEN1* or the D385A variant were transiently transfected with cDNA encoding APP WT. Note that the hyperphosphorylation of endogenous tau in primary neurons was markedly attenuated when the recipient cells were cocultured with the donor cells expressing *PSEN1* D385A, which inhibits Aβ production.

(B) Results of semiquantitative analysis of AT8/Tau-5 (total tau) are shown (n=4). *P<0.05 by Student's *t* test.

Supplementary Fig. 4

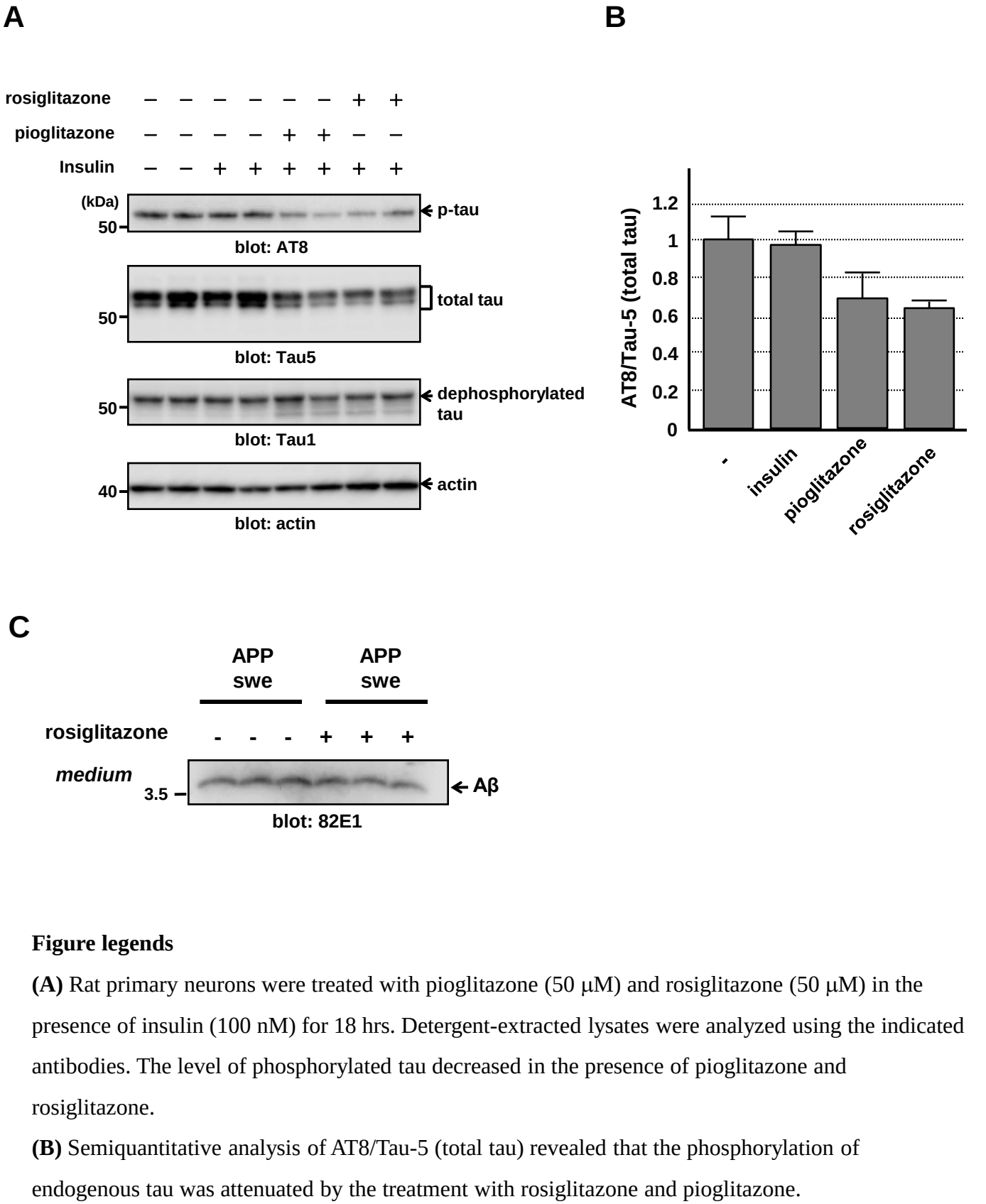

Figure legends

(A) Rat primary neurons were treated with pioglitazone (50 μM) and rosiglitazone (50 μM) in the presence of insulin (100 nM) for 18 hrs. Detergent-extracted lysates were analyzed using the indicated antibodies. The level of phosphorylated tau decreased in the presence of pioglitazone and rosiglitazone.

(B) Semiquantitative analysis of AT8/Tau-5 (total tau) revealed that the phosphorylation of endogenous tau was attenuated by the treatment with rosiglitazone and pioglitazone.

(C) Treatment with rosiglitazone does not affect the level of Aβ in the medium.

Supplementary Fig. 5

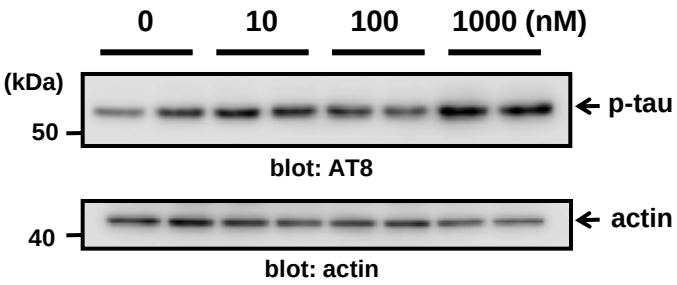

Figure legends

Rat primary neurons were treated with synthetic Aβ42 peptides at different concentrations. Detergent-extracted lysates were analyzed using the indicated antibodies. Synthetic Aβ42 peptides are required at ~1 μM to induce aberrant hyperphosphorylation of endogenous tau in primary neurons.